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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,586	11/30/2000	Michael Kock	49100	5846

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/13/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,586	KOCK ET AL.	
	Examin r	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *5-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 November 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The art unit location of your application and examiner has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1652, Examiner Richard Hutson Ph.D.

Applicants preliminary amendment of claims 1 and 2, paper No. 12, 10/25/2002, is acknowledged. Claims 1-32 are still at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, and SEQ ID NO: 2, Claims 1-4 in Paper No. 12 is acknowledged. In response to the restriction applicants have amended the claims and traverse the restriction based on applicant's amendment. Applicant's traversal is on the ground(s) that claim 1 is the only independent claim at issue, and as amended, this claim is drawn to an amino acid sequence comprising a functional NAD+ binding domain with the sequence $PX_n(S/T)GX_3GKGIYFA$, and lacking any zinc finger motif with the sequence $CX_2CX_MHX_2C$, wherein M is 28 or 30, and that such PARP homologs are not known in the prior art. This argument is not found persuasive because Magnus Johansson, Genomics 57 pages 442-445, teach the cloning of two PARP homologues, PARP-2 and PARP-3, each of which comprise a functional NAD+ binding domain with the sequence $PX_n(S/T)GX_3GKGIYFA$, and lack a zinc finger motif with the sequence $CX_2CX_MHX_2C$, wherein M is 28 or 30. Applicants further argue that each of the groups I-XV contain claims dependent on newly amended claim 1, either directly or indirectly, and applicants are technically entitled to have all of the present

claims examined during the present prosecution, especially those grouped as Groups I, V, VI, VII, XIII, and XIV. This argument is not found persuasive on the basis that even if the asserted "technical feature" of Group I was a "special technical feature", it is not shared by Groups V, VI, VII, XIII, and XIV, as was previously pointed out.

It is further noted that the previous restriction requirement did not include a species election requirement, but rather was only a restriction requirement. Applicants election of Group I and SEQ ID NO: 2 is treated as a response to this restriction requirement.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-32 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 12.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Applicants filing of information disclosures, Paper No. 5, filed 1/18/2001, is acknowledged. Those references considered have been initialed. Applicants attention

is directed to the reference Kupper et al., which does not include the appropriate Journal, Volume and page information. It is requested that this information be added.

Drawings

The drawings filed on 11/30/2002 are objected to for the reasons stated on the enclosed from PTO-948. Note, applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Specification

The disclosure is objected to because of the following informalities:

Figure 1 contains a number of sequence disclosures. As per M.P.E.P. 2422.02 -*The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures*, it should be noted, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings.

The specification appears to **not** contain all section headings (i.e. Detailed Description of the Invention, Description of Figures, etc...). These would be helpful. Applicant is referred to M.P.E.P. Section 601, GUIDELINES FOR DRAFTING A NONPROVISIONAL PATENT APPLICATION UNDER 35 U.S.C. 111(a).

As discussed above, under information disclosure statement, the reference Kupper et al., does not include the appropriate Journal, Volume and Page information. It is requested that this information be added.

Appropriate correction is required.

Claim Objections

Claims 1 and 4 are objected to because of the following informalities:

Claims 1 recites "$CX_2CX_MHX_2C$ (SEQ ID NO: 30) in which **m** is an integral..." . It is suggested that this be amended such that consistency is maintained in the case of the letters, such as "$CX_2CX_mHX_2C$ (SEQ ID NO: 30) in which **m** is an integral..."

Claim 4 contains non-elected subject matter (i.e. SEQ ID NO:s 4, 6, 8 and 10).

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter. In the absence of the hand of man, naturally occurring proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated and purified poly(ADP-ribose) polymerase ..." .

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (2-4 dependent on) is indefinite in that it is unclear if the limitations listed as "a)" and "b)" are intended to be limitations of the claimed "PARP homolog and the functional equivalents thereof" or are these intended to be limitations of "PARP". For the purpose of compact prosecution, the limitations "a)" and "b)" are intended to be limitations of the claimed "PARP homolog and the functional equivalents thereof".

Claim 1 is further indefinite in the recitation "...and the functional equivalents thereof". It is unclear what this phrase adds to the claim, given the above interpretation of the limitations of "a)" and "b)" as limiting the claimed molecule. What is the difference between a PARP homolog and a functional equivalent thereof, given that each must include the limitations of "a)" and "b)" as discussed above.

Claim 1 and 4 recitation of the phrase "functional equivalents thereof" which renders the instant claims vague and indefinite. A functional polypeptide may encompass a variety of different biological activities. These include but are not limited to immunological activity, such as acting as an antigen for an antibody; regulatory activity, such as that exhibited by many proteins which control transcription and/or

translation of not only their encoding nucleic acids but other nucleic acids as well; or enzymatic activity, for example, polymerase activity.

Claim 4 is indefinite in that it is drawn to a PARP homolog as claimed in claim 1, selected from human PARP homolog which has the amino acid sequence shown in SEQ ID NO: 2 (human PARP2) and the functional equivalents thereof. Claim 4 which depends from claim 1, and includes all of the limitations of claim 1 is further drawn to the functional equivalents thereof, is broader then claim 1 from which it depends.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4 are directed to all possible poly(ADP-ribose) polymerase (PARP) homologs and functional equivalents thereof, comprising a functional NAD^+ binding domain with the sequence $PX_n(S/T)GX_3GKGIYFA$, and lacking any zinc finger motif with the sequence $CX_2CX_MHX_2C$, wherein M is 28 or 30 (See above 112 second paragraph rejection) (claim 1), wherein said PARP homologs NAD^+ binding domain further comprises at least one of SEQ ID NOs: 12 or 13 (claim 2), wherein said PARP homolog further comprises at least one of SEQ ID NOs: 15-19 (claim 3), wherein said PARP

homolog has the amino acid sequence of SEQ ID NO: 2 and functional equivalents thereof (claim 4). The specification, however, only provides the representative species of SEQ ID NOs: 2, 4, 6, 8 or 10, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these PARP homologs or functional equivalents thereof by any identifying structural characteristics or properties, for which no predictability is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a poly(ADP-ribose) polymerase (PARP) homolog comprising the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any poly(ADP-ribose) polymerase (PARP) homolog and functional equivalents thereof, comprising a functional NAD^+ binding domain with the sequence $PX_n(S/T)GX_3GKGIYFA$, and lacking any zinc finger motif with the sequence $CX_2CX_MHX_2C$, wherein M is 28 or 30. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-4 are so broad as to encompass any poly(ADP-ribose) polymerase (PARP) homolog and functional equivalents thereof, comprising a functional NAD^+ binding domain with the sequence $PX_n(S/T)GX_3GKGIYFA$, and lacking any zinc finger motif with the sequence $CX_2CX_MHX_2C$, wherein M is 28 or 30 (See above 112 second paragraph rejection) (claim 1), wherein said PARP homolog's NAD^+ binding domain further comprises at least one of SEQ ID NOs: 12 or 13 (claim 2), wherein said PARP homolog further comprises at least one of SEQ ID NOs: 15-19 (claim 3),and wherein said PARP homolog has the amino acid sequence of SEQ ID NO: 2 and functional equivalents thereof (claim 4). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims, including all poly (ADP-ribose) polymerases with the specified limitations and functional equivalents thereof. The claims rejected under this section of U.S.C. 112, first paragraph, place minor if any

structural limits on the claimed molecules. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to those poly(ADP-ribose) polymerases (PARP) comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8 or 10.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any poly(ADP-ribose) polymerase because the specification does not establish: (A) regions of the protein structure which may be modified without effecting polymerase activity; (B) the general tolerance of poly(ADP-ribose) polymerases to modification and extent of such tolerance; (C) a

rational and predictable scheme for modifying any amino acid residue of a poly(ADP-ribose) polymerase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the poly(ADP-ribose) polymerase activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any poly(ADP-ribose) polymerase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by Johansson (Genomics, Vol 57, pages 442-445, May 1999).

Johansson teach the identification and cloning two human poly(ADP-ribose) polymerase, designated PARP-2 and PARP-3. Johansson teach the amino acid sequence of PARP-2 and PARP-3 and teach that each of these comprise a NAD+ binding domain which has the amino acid sequence of SEQ ID NO: 11, but do not comprises SEQ ID NO: 30. Johansson further teach that these PARP proteins comprise either SEQ ID NO: 12 (PARP-3) or 13 (PARP-2) and at least one of SEQ ID NO:s 15-19. Thus Johansson anticipates claims 1-4.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Thibodeau et al. (Biochem. Cell Biol, Vol 67, pages 653-660, 1989).

Thibodeau et al. teach the cloning of a rodent cDNA encoding the poly(ARP) polymerase catalytic domain. The encoded protein comprises a NAD^+ binding domain which has the amino acid sequence of SEQ ID NO: 11, but does not comprises SEQ ID NO: 30. The encoded protein further comprises the amino acid sequence of SEQ ID

NO: 12 and SEQ ID NO: 18 and is a functional equivalent of SEQ ID NO: 2. Thus Thibodeau et al. anticipates claims 1-4.

Remarks

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
January 10, 2003